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10/570,159	03/01/2006	Noboru Fukuda	0152-0725PUS1	4886
2292 7590 02/22/2010 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747				
EXAMINER				
HEARD, THOMAS SWEENEY				
ART UNIT		PAPER NUMBER		
1654				
NOTIFICATION DATE		DELIVERY MODE		
02/22/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary

Application No.

10/570,159

Applicant(s)

FUKUDA ET AL.

Examiner

THOMAS S. HEARD

Art Unit

1654

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 0209.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 5-9 is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 3/1/2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SI.08)
- Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The Applicants Amendments to the claims received on 12/03/2009 is acknowledged. The text of those sections of Title 35 U.S. Code not included in the action can be found in the prior office action. Rejections or objections not addressed in this office action with respect to the previous office action mailed 9/3/2009 are hereby withdrawn.

Claim(s) 1-9 are pending. Applicants have amended claim(s) 1, 3, 4, and 5.
Claims 1-9 are hereby examined on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

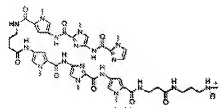
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by White et al., Chemistry & Biology, Vol. 4, No. 8,569-578, (1997), from Applicant's submitted ID.

The instant invention is drawn to a TGF-Beta gene expression inhibitor comprising a pyrrole-imidazole polyamide containing: an N-methylpyrrole unit (hereinafter also referred to as Py), an N-methylimidazole unit (hereinafter also referred to as Im) and a gamma-aminobutyrate unit, wherein said pyrrole-imidazole polyamide can be folded into a U-shaped conformation at the γ -aminobutyrate unit.

White et al discloses the following structure:



. This structure has a gamma-aminobutyrate moiety ($-\text{NH}-(\text{CH}_2)_3-\text{C}(\text{O})-$) as noted in the turn of the structure on the left, and also comprises a beta-alanine unit ($-\text{NH}-(\text{CH}_2)_2-\text{C}(\text{O})-$) at the tail end of the molecule.

Because the structural limitations of Claims 1 and 2 are fully met, the properties:

(1) can be folded into a U-shaped conformation at the γ -aminobutyrate unit in a minor groove of a double helix region (hereinafter referred to as target region) which comprises a part or all of the following base sequence from -557 to -536 (SEQ ID NO: 1) in a human transforming growth factor 131 (hereinafter also referred to as hTGF β 1) promoter, and a complementary strand thereof: TAAAGGAGAGCAATTCTTACAG wherein a Py/Im pair corresponds to a C-G base pair, an Im/Py pair corresponds to a G-C base pair, and a Py/Py pair corresponds to both an A-T base pair and a T-A base pair, or

(2) the TGF-13 gene expression inhibitor according to claim 1 or 2, wherein said target region is a double helix region comprising a part or all of the following base sequence from -548 to -537 (SEQ ID NO: 2) in the hTGF-131 promoter, and a complementary strand thereof, GCAATTCTTACA, or

(3) the TGF-13 gene expression inhibitor according to claim 1 or 2, wherein said target region is a double helix region comprising a part or all of the following base sequence from -548 to -537 (SEQ ID NO: 2) in the hTGF-131 promoter, and a complementary strand thereof, GCAATTCTTACA,

from Claims 1, 3, and 4 respectively, must be inherent in the structure. Therefore, the invention as claimed is anticipated by the prior art.

Applicant's Arguments

Applicants have argued:

(1) The Examiner states that White et al. reference describes a polyamide that can fold in a minor groove of the double helix region of SEQ. ID. NO. 1 (-557 to -536). The Examiner also indicates that the structure of a polyamide is disclosed in White et al. However, White et al. do not describe or suggest the pyrrole-imidazole polyamide as instantly claimed. The targeted sequence is even different in White et al. versus that of the present invention. Applicants also note the changes to claim 1 as shown herein.

(2) In this regard: "Because the hallmark of anticipation is prior invention, the prior art reference--in order to anticipate under 35 U.S.C. §102--must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim.'" *Net MoneyIN Inc. v. VeriSign Inc.*, 545 F.3d 1359, 88 USPQ2d 1751, 1758 (Fed. Cir. 2008) (citing *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983)). The White et al. reference fails to disclose all claimed features as explained above. Applicants traverse any assertion of inherency as well due to the different disclosure in White et al.

(3) Still, the Examiner states that White et al. disclose a polyamide structure having "a Py/Im pair corresponds to a C-G base pair, an Im/Py pair corresponds to a G-C pair, and a Pyr/Pyr pair corresponds to both an A-T and a T-A base pair." However, since the targeted sequences of White et al. and the present invention are different and the polyamide should be designed based on the corresponding pairs as mentioned above, the polyamide of the present invention is different from that of White et al. Accordingly, even if White et al. disclose corresponding base pairs, White et al. would still not disclose all claimed features. In summary, it is respectfully submitted that the Examiner has not presented a prima facie case of anticipation because (1) the specifically exemplified embodiments of the present invention are considerably different from the exemplified embodiments in the prior art and (2) the stated function (target region) in the prior art is different from the stated function (target region) of the present invention. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Response to Applicants Arguments

Applicants arguments have been carefully considered but are not deemed persuasive to overcome the rejection. The Applicants are claiming the invention by what it does rather than what it is. The examiner found a pyrrole imidazole polyamide and a gamma aminobutyrate unit. The remaining language of Claim 1 is functional language. Applicants have not claimed a product in a manner that overcomes the rejection nor describes the compound in a manner that describes a compound in a clear and distinct

manner, as in Claims 5 for example. Since the limitations of the components of the compound have been met, the functional language has also been met as being inherent in the compound. The compound of White et al is completely within the language of Claims 1, as well as thousands of others. The language of Claim 1 is to a genus of compounds, not a single compound of Claims 5, for example. Lastly, regarding (3), "prima facie case of anticipation is not understood, as this language as prima facie case is usually made in the context of a 103a) rejection. Further, Applicants assertion that the *"specifically exemplified embodiments of the present invention are considerably different from the exemplified embodiments of the prior art"* is incorrect. Applicants have only one embodiment. That embodiment is claimed as a genus of three components of the single compound. Those components have been found is a single compound and is, therefore, prior art. The rejection stands for reasons stated supra.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed.

The factors considered in the Written Description requirement are:

- (1) level of skill and knowledge in the art,
- (2) partial structure,
- (3) physical and/or chemical properties,
- (4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and
- (5) the method of making the claimed invention.

In the instant case, the claims are drawn to a TGF-beta gene expression inhibitor comprising a pyrrole-imidazole polyamide containing: an N-methylpyrrole unit (hereinafter also referred to as Py), an N-methylimidazole unit (hereinafter also referred to as Im) and gamma-aminobutyrate unit, wherein said pyrrole-imidazole polyamide can be folded into a U-shaped conformation at the gamma-aminobutyrate unit in a minor groove of a double helix region (hereinafter referred to as target region) which comprises a part or all of the following base sequence from -557 to -536 (SEQ ID NO: 1) in a human transforming growth factor 131 (hereinafter also referred to as hTGFβ1) promoter, and a complementary strand thereof:
TAAAGGAGAGCAATTCTTACAG

wherein a Py/Im pair corresponds to a C-G base pair, an Im/Py pair corresponds to a G-C base pair, and a Py/Py pair corresponds to both an A-T base pair and a T-A base pair..

(1) Level of skill and knowledge in the art:

The level of skill to practice the art of the instantly claimed invention is high with regard to synthesis, isolation, structure analysis of the compounds, bioassays and structure function assay are all high skill techniques and require broad knowledge in the field.

(2) Partial structure: (3) Physical and/or chemical properties: and (4) Functional characteristics:

The structural components are those of pyrrole-imidazole (Im-Py) used in making repeating units that intercalate to specific sequences of DNA.

(5) Method of making the claimed invention:

Standard nucleic acid synthesis known in the art.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that Claim(s) 1- 4 are a broad generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of compound that can specifically bind all or part of SEQ ID NO:1-3.

It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163.

Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. There is one example and while having written description for that specific example there is insufficient description of a DNA sequence to which either the specific Im/Py containing structure, or the broad generic Im/Py structures would bind, and that would allow one of skill in the art to practice the invention as claimed. There has been no guidance provided on how to combine the Im and Py units along with the beta-alanine and gamma-aminobutyrate moieties such that one of ordinary skill in the art would know what correlates the structure to function. The language of Claim 1 is more functional than structure. The skilled artisan what not to what make in order to have the function. Given that it binds a specific sequence, it is unclear how such a broad Claim to a broad genus could perform such a specific task of binding the specific sequences claimed. Claim 1 is almost all functional in language and only provides the components of the compound and not what the whole compound is. It is more akin to a game of "molecular charades" where components of the compound are named and the function of the undescribed compound is listed, and the skilled artisan is left to guess what the whole of the molecule is.

Further, 37 CFR 1.57(c) states that "Essential material" may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication, which patent or patent application publication does not

itself incorporate such essential material by reference. "Essential material" is material that is necessary to:

- (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;
- (2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or
- (3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112.

The specification does not clearly teach the structure function relationships such the one of ordinary skill in the art is informed of this relationship, and also demonstrate that applicants are in possession of the full genus of Claims 1-4

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Conclusion

Claims 5-9 are allowed. No other claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Thomas S. Heard** whose telephone number is **(571) 272-2064**. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

/Thomas S Heard/
Examiner, Art Unit 1654

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